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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/202,455	12/15/98	YAMAGUCHI K	FJN-070

HM22/0225

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BOSTON MA 02110

EXAMINER	
HAMUD, F	
ART UNIT	**PAPER NUMBER**
1646	10

DATE MAILED: 02/25/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

FILE COPY

Office Action Summary

Application No.	Applicant(s)
09/202,455	Yamaguchi et al
Examiner	**Group Art Unit**
Fozia Hamud	1646

☒ Responsive to communication(s) filed on *Jan 3, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-64* is/are pending in the application.

Of the above, claim(s) *2-7, 17-20, 32-35, and 45-64* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 8-16, 21-31, and 36-44* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1a. Claims 12, 13, 16-20, 24-28, 30-35, 38-41, 43-48, 57 and 60-64 have been amended in Paper No.3, filed on 12/15/98.

1b. Applicant's election with traverse of Group I (claims 1, 8-16, 21-31 and 36-44) in Paper No.9 filed on January 3, 2000 is acknowledged.

The traversal is on the grounds that a search for one Group would necessarily include a search in the classes and subclasses relevant to the other groups.

This traversal is not found persuasive because, firstly, this application is a 371 of PCT/EJP98/01728, therefore, PCT rules for lack of unity were followed rather than US restriction rules. Thus, the inventions listed as Groups I-V do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical feature for the reasons set forth in the office action mailed on November 4, 1999 in Paper No.6. Secondly, even if US restriction rules were to be followed, the inventions of Groups I-V would have been classified in different classes and sub-classes, and since each distinct subject has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search, a search for one Group would not necessarily have revealed pertinent art on any of the other groups. See (MPEP § 808.02)

The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 2-7, 17-20, 32-35 and 45-64 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Specification

2a. The Drawings have been approved by the draftsman.

2b. It is noted that this application appears to claim subject matter disclosed in prior PCT Application No. PCT/EP97/001728, now WO 98/46644, filed on 04/15/98. A reference to the prior application must be inserted as the first sentence of the specification of this application if Applicant intends to rely on the filing date of the prior application under 35 U.S.C. 120. See 37 CFR 1.78(a). It is suggested that below the title of the invention be inserted:

Cross Reference to Related Applications

"This Application is a 371 of WO 98/46644".

Appropriate correction is required.

2b. The abstract of the disclosure is objected to, because it comprises three paragraphs. It is required that the abstract be limited to a single paragraph within the range of 50 to 250 words. Correction is required. See MPEP § 608.01(b).

2c. The title of the invention is objected to, because the word "novel" is not considered as part of the title of an invention and the Patent and Trademark Office does not include such words at the beginning of the invention. A title without the word "Novel" is suggested . See §M.E.P. 606.01.

2d. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 U.S.C. § 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3a. Claims 1, 8-15, 21-30, 36-43 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1, 8-15, 21-30, 36-43 recite "a protein having.... or a DNA encoding the amino acid sequence...." which encompass the protein and the DNA as they occur in nature. However, since Applicants do not intend to claim a naturally occurring product amendment of the claims to show the hand of man would obviate this rejection. It is suggested that the claims be amended to recite " an isolated protein..... or an isolated DNA comprising .....". Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claims 1, 12, 21, 23-24, 26-31, 36-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:11, said polypeptide which is encoded by a polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO:2 or SEQ ID NO:12 respectively, and a fragment of the polypeptide of SEQ ID NO:1 comprising amino acid residues 72-316 or 76-316, and a method of recombinantly making said polypeptides, is not enabling for a "all" possible proteins having the activity and features recited in claim 1, or a polynucleotide having 70% or more homology to the polynucleotide of SEQ ID Nos:2 or SEQ ID Nos:12, or "all" possible polynucleotides encoding the polypeptides of SEQ ID Nos: 1 or 11. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 recites "a protein having the following physicochemical characteristics: binds to OCIF, comprises molecular weight of 30,000-40,0000, supports or promotes osteoclasts differentiation and maturation...", what is claimed in claim 1 broadly encompasses "all" proteins that exhibit the features recited, while the specification discloses a mouse polypeptide comprising the amino acid sequence set forth in SEQ ID NO:1 and a human polypeptide comprising the amino acid sequence set forth in SEQ ID NO:11, said proteins produced recombinantly or produced and purified from osteoblaststic stromal cells, bind to labeled OCIF, comprise apparent molecular weight of 30,000 to 40,000 Daltons and promote osteoclasts differentiation and maturation (see pages 53, 67 and 85, 108 and Figures 1, 2, and 26), the specification is non-enabling for the unlimited number of proteins having this property, and which are encompassed by the scope of the claims. Also the instant specification is non-enabling for "all" possible proteins that promote osteoclasts differentiation and maturation in a co-culture system, in the presence of active form of vitamin D_3 and parathyroid hormone.

With respect to claims 12, 27 and 40, which recite " a DNA having 70% or more homology to a DNA encoding .....", the specification does not provide the requisite examples nor a representative number of different sequences that would allow the skilled artisan to produce a polynucleotide having 70% or more sequence identity to, for example, the polynucleotide encoding the polypeptide with the amino acid sequence set forth in SEQ ID NO:1, nor does the disclosure provide criteria that explicitly enable such critical features. Furthermore, in the absence of a sufficient

number of examples to enable the scope of the claims, the specification fails to provide the necessary guidance with assurance that one of ordinary skill in the art would obtain the products that possess the desired properties. Claims 12, 27 and 40 are overly broad in the recitation of "70% or more homology" since no guidance is provided as to which of the myriad of polynucleotide species encompassed by the claims would encode the desired polypeptide of SEQ ID NO:1, therefore, the claims broadly encompass a significant number of inoperative species. In the specification (pages 15-30), Applicants describe the isolation, expression and sequence determination of cDNAs encoding human and mouse proteins which specifically bind to OCIF. However, there is no disclosure of any variants or analogs of the human or mouse polypeptide. There is no guidance in the specification as to how one of ordinary skill in the art would generate a polynucleotide or a polypeptide encoded thereby, other than that exemplified. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. The instant claims are not limited to naturally-occurring compounds and the instant specification does not provide a description of a repeatable process of producing a polynucleotide which deviates from the disclosed sequence (SEQ ID NO:2 or 12) by as much as 30%,

which encodes the polypeptide with the amino acid sequence set forth in SEQ ID NO:1 or 11. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those nucleotide of the disclosed naturally-occurring polynucleotide, which are required to encode a functional protein. It is this additional characterization of the disclosed polynucleotide that is required in order to obtain the functional and structural data needed to permit one to produce a polypeptide which meets both the structural and functional requirements of the instant claim that constitutes undue experimentation.

The instant specification does not provide the guidance needed to predictably alter by 30%, of the polynucleotide of SEQ ID No:2 or 12, which would encode a polypeptide with the amino acid sequence depicted in SEQ ID NO:1 or 11 respectively, with any reasonable expectation that the resulting protein will have the desirable activity, for example bind to OCIF. The instant specification does not outline residues which are considered conservative. This is not adequate guidance as to the nature of the analogues or variants of the nucleic acid molecules that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Also with respect to claims drawn to DNA with one or more nucleotide deleted, substituted, added or inserted, the specification does not demonstrate exactly where these changes, (deletions, additions etc) are to be made in the polynucleotide, if these changes are conservative or not, would these changes result in change in the encoded amino acids, and if so are these amino acid changes conservative or not. To illustrate this point, the Examiner has cited George et al. (1988) which discloses that "sequence-comparison methods will not be able to assess biological relatedness

until the structure/function problem is more clearly understood" (see page 145, last 4 lines of column 2) and that "statistical measures of similarity do not necessarily reflect biological significance" (see page 146, column 1, lines 11-13). Therefore Applicants have not presented enablement commensurate in scope with the claims.

With respect to claims reciting fragments the only fragments enabled by the instant specification are the fragments comprising amino acid residues 72-316 or 76-316 of the polypeptide of SEQ ID NO:1, and not "all" possible fragments as recited in the claims.

With respect to claim 10 which recites "a DNA .....encoding a protein capable of specifically binding to OCIF .. .. . " The specification is non-enabling for a protein that does not bind to OCIF and is capable of binding to it, only if further modified, since Applicants have not taught how to further modify the protein such that it can bind to OCIF. It has been held that an element is "capable of' performing a function is not a positive limitation but only requires the ability to perform. It does not constitute a limitation in any patentable sense. In re Hutchison, 69 USPQ 138.

4b. Claims 21-23, 30, 36 and 43, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only discloses the isolated protein comprising the amino acid sequence set forth in SEQ ID NO:1 or 11, and therefore the written description is not commensurate in scope with the claims drawn to variants or analogues of the protein with the amino acid sequence set forth of SEQ ID NO:1 or 11 as recited in claims 21-23, 30, 36 and 43.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO: NO:1, 3-6, 8, 11, the skilled artisan cannot envision the detailed structure of the encompassed polypeptide or the polynucleotide encoding such and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Applicants describe the isolation, expression and sequence determination of human and mouse proteins which specifically bind to OCIF. However, there is no disclosure of variants or analogs of the mouse or human protein comprising the amino acid sequence set foeth in SEQ ID NO:1 or 11.

Therefore only isolated polypeptide comprising the amino acid sequence of SEQ ID NO:1, or 11, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph. As a result, it does not appear that the inventors were in possession of variants or analogues or fragments (with the exception of the fragment comprising amino acid residues 72-316 or 76-316 of the polypeptide of SEQ ID NO:1), of the polypeptides of SEQ ID NO:1 or 11.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5a. Claims 1, 10-14, 21-231, 36-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5b. Claim 1 is vague and indefinite for the recitation of ".....kd = 10^{-9} M or less ....", in sub-part a, which renders the claims indefinite because how much "less" should the kd of the claimed protein be from 10^{-9} M, 10^{-10} M, 10^{-12} M or something else?. The metes and bounds of the claim is not ascertainable. Claim 1 also recites "...supporting or promoting osteoclasts differentiation and maturation...", the term "supporting" renders the claim vague, because it is unclear if the claimed protein sufficiently promotes osteoclasts differentiation and maturation by itself, or if it only plays a supporting role in the presence of other agents that promote osteoclasts differentiation and maturation. Appropriate correction is required.

5c. Regarding claim 1 the phrase "such as" renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

5d. Claim 10, recites "a DNA with one or more nucleotides deleted, substituted, added or inserted", which render the claim indefinite because it is unclear how many nucleotide deletions, substitutions, additions or insertions should be made, 1, 100, 1000 or something else? It is also unclear where in the polynucleotide of SEQ ID NO:2, should these changes be made, within the coding region, outside the coding region?. Appropriate correction is required.

5e. Regarding claims 11, 26, 39, the phrase "relatively mild conditions" renders the claims indefinite because it is unclear how mild should the hybridization conditions be, or mild relative to what conditions? This rejection could be obviated by supplying specific conditions supported by the specification which Applicants consider to be "mild."

5f. Regarding claims 21-23, 30, 36, 41, 43, the phrase "including" renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

5g. Claims 12, 27, 40, recite "70% or more homology", which renders the claims indefinite because it is unclear what should the % homology between the claimed DNA and the DNA molecule with the nucleotide sequence set forth in SEQ ID NO:2 have, 71%, 99% or something else? Appropriate correction is required.

5h. Claim 15 recites the limitation "the protein having.... " in line 1. There is no antecedent basis for "the protein" in the claim. Approoriate correction is required.

5i. Claims 8-9, 15, 25, 30, 36, 38 and 43 recite "....sequence ID NO. 1 in sequence table", to identify polynucleotides or polypeptides, however, it is suggested that the polynucleotides or the polypeptides be identified only by SEQ ID No: followed by the appropriate number, e.g SEQ ID NO:1, and the recitation of the sequence table be removed. A

All the claims that depend on the claims rejected under 112, second paragraph are also rejected as being vague and indefinite.

Claim Rejections - 35 U.S.C. § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. Claims 1, 8-16, 21-31, 36, 39-41, 43-44 are rejected under 35 U.S.C. 102(e) as being anticipated by Boyle (US Patent 5,843,678).

Boyle teaches an isolated murine nucleic acid molecule encoding a protein, that specifically binds to osteoprotegrin (OPG), an expression vector comprising said nucleic acid molecule and a method of making the encoded protein, (see column 3, lines 15-60, and Example 2). The protein disclosed by Boyle comprises 316 amino acid in length, has amino acid terminal cytoplasmic domain, a transmembrane domain and a carboxyl terminal extracellular domain, and is involved in osteoclast differentiation, (see column 2, lines 20-55). The OPG binding protein disclosed by Boyle may be membrane-associated or may be in soluble form.

The polynucleotide disclosed by Boyle shares 100% identity to instantly claimed polynucleotide sequence of SEQ ID NO: 2, and encodes a polypeptide which shares 100% identity to the polypeptide of SEQ ID NO:1 of the present invention. See attached copies of the comparison of SEQ ID NO:2 and SEQ ID NO:1 claimed in the instant invention and the sequences of the reference (SEQUENCE COMPARISON 'A' and 'B', respectively). Therefore Boyle's reference clearly anticipates the instant claims 1, 8-16, 21-31, in the absence of any evidence to the contrary.

With respect to the limitation "a DNA which hybridizes under mild hybridization...." recited in claims 11 and 26, the polynucleotide of Boyle would be expected to hybridize completely to the instant claimed polynucleotide under any hybridization conditions.

With respect to claim 24, the protein disclosed by Boyle would be expected to have an inhibitory effect on osteoprotegerin/osteoclastogensis inhibitory factor (OPG/OCIF), since it binds to said protein.

The polynucleotide disclosed by Boyle shares 69.7% with the polynucleotide of SEQ ID NO:12 of the instant invention. The polynucleotide disclosed by Boyle meets the limitation of "a DNA having 70% or more homology..." recited in claim 40, because the polynucleotide disclosed by Boyle shares 82.4% similarity with certain regions of the polynucleotide of SEQ ID NO:12. See attached copies of the comparison of SEQ ID NO:12 claimed in the instant invention and the sequences of the reference (SEQUENCE COMPARISON 'C'). It also meets the fragment limitation recited in claims 36 and 43, because the polynucleotide of Boyle would be expected to encode a fragment of the polypeptide of SEQ ID NO:11. The Boyle reference also anticipates claims 41 and

44, because it teaches a method of expressing and purifying the protein encoded by their polynucleotide.

With respect to the limitation "a DNA which hybridizes under mild hybridization...." recited in claim 39 the polynucleotide of Boyle would be expected to hybridize under mild conditions to the instant claimed polynucleotide.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8896. The examiner can normally be reached on Monday-Friday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1646
February 23, 2000

Prema Mertz
PREMA MERTZ
PRIMARY EXAMINER

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US-08-842-842-6
; Sequence 6, Application US/08842842
; Patent No. 5843678
; GENERAL INFORMATION:
;   APPLICANT:  Boyle, William J.
;   TITLE OF INVENTION:  OSTEOPROTEGERIN BINDING PROTEINS
;   NUMBER OF SEQUENCES:  7
;   CORRESPONDENCE ADDRESS:
;     ADDRESSEE:  Amgen Inc.
;     STREET:  1840 Dehavilland Drive
;     CITY:  Thousand Oaks
;     STATE:  California
;     COUNTRY:  USA
;     ZIP:  91230-1789
;   COMPUTER READABLE FORM:
;     MEDIUM TYPE:  Floppy disk
;     COMPUTER:  IBM PC compatible
;     OPERATING SYSTEM:  PC-DOS/MS-DOS
;     SOFTWARE:  PatentIn Release #1.0, Version #1.30
;   CURRENT APPLICATION DATA:
;     APPLICATION NUMBER:  US/08/842,842
;     FILING DATE:
;     CLASSIFICATION:  435
;   ATTORNEY/AGENT INFORMATION:
;     NAME:  Winter, Robert B.
;     REFERENCE/DOCKET NUMBER:  A-451
;  INFORMATION FOR SEQ ID NO:  6:
;   SEQUENCE CHARACTERISTICS:
;     LENGTH:  2295 base pairs
;     TYPE:  nucleic acid
;     STRANDEDNESS:  single
;     TOPOLOGY:  linear
;   MOLECULE TYPE:  cDNA
;   FEATURE:
;     NAME/KEY:  CDS
;     LOCATION:  158..1105
US-08-842-842-6

  Query Match             100.0%;  Score 1538;  DB 3;  Length 2295;
  Best Local Similarity   100.0%;  Pred. No. 0:
  Matches 1538;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps

Qy       1 gccaggacctctgtgaaccggtcggggcgggggccgcctggccgggagtctgctcggcgg 60
Db      34 GCCAGGACCTCTGTGAACCGGTCGGGGCGGGGGCCGCCTGGCCGGGAGTCTGCTCGGCGG 93

Qy      61 tgggtggccgaggaagggagagaacgatcgcggagcagggcgcccgaactccgggcgccg 120
Db      94 TGGGTGGCCGAGGAAGGGAGAGAACGATCGCGGAGCAGGGCGCCCGAACTCCGGGCGCCG 153

Qy     121 cgccatgcgccgggccagccgagactacggcaagtacctgcgcagctcggaggagatggg 180
Db     154 CGCCATGCGCCGGGCCAGCCGAGACTACGGCAAGTACCTGCGCAGCTCGGAGGAGATGGG 213

Qy     181 cagcggccccggcgtcccacacgagggtccgctgcaccccgcgccttctgcaccggctcc 240
Db     214 CAGCGGCCCCGGCGTCCCACACGAGGGTCCGCTGCACCCCGCGCCTTCTGCACCGGCTCC 273

Qy     241 ggcgccgccacccgccgcctcccgctccatgttcctggccctcctggggctgggactggg 300
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Qy     301 ccaggtggtctgcagcatcgctctgttcctgtactttcgagcgcagatggatcctaacag 360
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Qy     361 aatatcagaagacagcactcactgcttttatagaatcctgagactccatgaaaacgcagg 420
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Qy     421 tttgcaggactcgactctggagagtgaagacacactacctgactcctgcaggaggatgaa 480
Db     454 TTTGCAGGACTCGACTCTGGAGAGTGAAGACACACTACCTGACTCCTGCAGGAGGATGAA 513
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Sequence Comparison A

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Title:
Perfect score:  1538
Sequence:  US-09-202-455-2

 1 gccaggacctctgtgaaccg.....ttttttctaatgaggagag 1538

Run on:  February 14, 2000, 21:27:57 ; Search time 99.67 Seconds
         (without alignments)
         1843.728 Million cell updates/sec

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Qy     601 tgaggcccagccatttgcacacctcaccatcaatgctgccagcatcccatcgggttccca 660
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Qy     661 taaagtcactctgtcctcttggtaccacgatcgaggctgggccaagatctctaacatgac 720
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Qy     841 gtatgtcgttaaaaccagcatcaaaatcccaagttctcataacctgatgaaaggagggag 900
Db     874 GTATGTCGTTAAAACCAGCATCAAAATCCCAAGTTCTCATAACCTGATGAAAGGAGGGAG 933

Qy     901 cacgaaaaactggtcgggcaattctgaattccacttttattccataaatgttgggggatt 960
Db     934 CACGAAAAACTGGTCGGGCAATTCTGAATTCCACTTTTATTCCATAAATGTTGGGGGATT 993

Qy     961 tttcaagctccgagctggtgaagaaattagcattcaggtgtccaaccccttccctgctgga 1020
Db     994 TTTCAAGCTCCGAGCTGGTGAAGAAATTAGCATTCAGGTGTCCAACCCTTCCCTGCTGGA 1053

Qy    1021 tccggatcaagatgcgacgtactttggggctttcaaagttcaggacatagactgagactc 1080
Db    1054 TCCGGATCAAGATGCGACGTACTTTGGGGCTTTCAAAGTTCAGGACATAGACTGAGACTC 1113

Qy    1081 atttcgtggaacattagcatggatgtcctagatgtttggaaacttcttaaaaaatggatg 1140
Db    1114 ATTTCGTGGAACATTAGCATGGATGTCCTAGATGTTTGGAAACTTCTTAAAAAATGGATG 1173

Qy    1141 atgtctatacatgtgtaagactactaagagacatggcccacggtgtatgaaactcacagc 1200
Db    1174 ATGTCTATACATGTGTAAGACTACTAAGAGACATGGCCCACGGTGTATGAAACTCACAGC 1233

Qy    1201 cctctctcttgagcctgtacaggttgtgtatatgtaaagtccataggtgatgttagattc 1260
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Qy    1261 atggtgattacacaacggttttacaattttgtaatgatttcctagaattgaaccagattg 1320
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Qy    1321 ggagaggtattccgatgcttatgaaaaacttacacgtgagctatggaaggggtcacagt 1380
Db    1354 GGAGAGGTATTCCGATGCTTATGAAAAACTTACACGTGAGCTATGGAAGGGGGTCACAGT 1413

Qy    1381 ctctgggtctaaccccctggacatgtgccactgagaaccttgaaattaagaggatgccatg 1440
Db    1414 CTCTGGGTCTAACCCCTGGACATGTGCCACTGAGAACCTTGAAATTAAGAGGATGCCATG 1473

Qy    1441 tcattgcaaagaaatgatagtgtgaagggttaagttcttttgaattgttacattgcgctg 1500
Db    1474 TCATTGCAAAGAAATGATAGTGTGAAGGGTTAAGTTCTTTTGAATTGTTACATTGCGCTG 1533

Qy    1501 ggacctgcaaataagttctttttttctaatgaggagag 1538
Db    1534 GGACCTGCAAATAAGTTCTTTTTTTCTAATGAGGAGAG 1571
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GenCore version 4.5
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OM protein - protein search, using sw model

Run on: February 15, 2000, 01:33:44 ; Search time 42.37 Seconds
(without alignments)
176.654 Million cell updates/sec

Title: US-09-202-455-1
Perfect score: 1675
Sequence: 1 MRRASRDYGKYLRSSEEMGS.....LLDPDQDATYFGAFKVQDID 316

Scoring table: BLOSUM62

Searched: 188963 seqs, 23686106 residues

Database : A_Geneseq_36:*

ALIGNMENTS

RESULT 1
US-08-842-842-7
; Sequence 7, Application US/08842842
; Patent No. 5843678
; GENERAL INFORMATION:
; APPLICANT: Boyle, William J.
; TITLE OF INVENTION: OSTEOPROTEGERIN BINDING PROTEINS
; NUMBER OF SEQUENCES: 7
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Amgen Inc.
; STREET: 1840 Dehavilland Drive
; CITY: Thousand Oaks
; STATE: California
; COUNTRY: USA
; ZIP: 91230-1789
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.30
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/842,842
; FILING DATE:
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Winter, Robert B.
; REFERENCE/DOCKET NUMBER: A-451
; INFORMATION FOR SEQ ID NO: 7:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 316 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-842-842-7

Sequence comparison B

Query Match 100.0%; Score 1675; DB 2; Length 316;
Best Local Similarity 100.0%; Pred. No. 1.8e-157;
Matches 316; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      61 VVCSIALFLYFRAQMDPNRISEDSTHCFYRILRLHENAGLQDSTLESEDTLPDSCRRMKQ 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy     121 AFQGAVQKELQHIVGPQRFSGAPAMMEGSWLDVAQRGKPEAQPFAHLTINAASIPSGSHK 180
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Db     121 AFQGAVQKELQHIVGPQRFSGAPAMMEGSWLDVAQRGKPEAQPFAHLTINAASIPSGSHK 180

Qy     181 VTLSSWYHDRGWAKISNMTLSNGKLRVNQDGFYYLYANICFRHHETSGSVPTDYLQLMVY 240
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Db     181 VTLSSWYHDRGWAKISNMTLSNGKLRVNQDGFYYLYANICFRHHETSGSVPTDYLQLMVY 240

Qy     241 VVKTSIKIPSSHNLMKGGSTKNWSGNSEFHFYSINVGGFFKLRAGEEISIQVSNPSLLDP 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 VVKTSIKIPSSHNLMKGGSTKNWSGNSEFHFYSINVGGFFKLRAGEEISIQVSNPSLLDP 300

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Db     301 DQDATYFGAFKVQDID 316
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RESULT 1
US-08-842-842-6
; Sequence 6, Application US/08842842
; Patent No. 5843678
; GENERAL INFORMATION:
; APPLICANT: Boyle, William J.
; TITLE OF INVENTION: OSTEOPROTEGERIN BINDING PROTEINS
; NUMBER OF SEQUENCES: 7
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Amgen Inc.
; STREET: 1840 Dehavilland Drive
; CITY: Thousand Oaks
; STATE: California
; COUNTRY: USA
; ZIP: 91230-1789
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.30
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/842,842
; FILING DATE:
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Winter, Robert B.
; REFERENCE/DOCKET NUMBER: A-451
; INFORMATION FOR SEQ ID NO: 6:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 2295 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: cDNA
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 158..1105
US-08-842-842-6

Sequence Comparison C

OM nucleic - nucleic search, using sw model

Run on: February 15, 2000, 00:20:43 ; Search time 89.6 Seconds
(without alignments)
2663.876 Million cell updates/sec

Title:
Perfect score: 954
Sequence: 1 atgcgccgcgccagcagaga.....aagttcgagatatagattga 954

Scoring table: IDENTITY_NUC

Searched: 311585 seqs, 125096042 residues

Query Match 69.7%; Score 664.6; DB 3; Length 2295;
Best Local Similarity 82.4%; Pred. No. 3.5e-170;
Matches 789; Conservative 0; Mismatches 159; Indels 9; Gaps 2;

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Db     158 ATGCGCCGGGCCAGCCGAGACTACGGCAAGTACCTGCCAGCTCGGAGGAGATGGGCAGC 217

Qy      61 ggccccggagccccgcacgagggccccctgcacgccccgc---cgccgcctgcgccgcac 117
Db     218 GGCCCCGGCGTCCCACACGAGGGTCCGCTGCACCCCGCGCCTTCTGCACCGGCTCCGGCG 277

Qy     118 cagccccctgccgcctcccgctccatgttcgtggccctcctgggggctgggcctgggcccag 177
Db     278 CCGCCACCCGCCGCCTCCCGCTCCATGTTCCTGGCCCTCCTGGGGCTGGGACTGGGCCAG 337

Qy     178 gttgtctgcagcgtcgccctgttcttctatttcagagcgcagatggatcctaatagaata 237
Db     338 GTGGTCTGCAGCATCGCTCTGTTCCTGTACTTTCGAGCGCAGATGGATCCTAACAGAATA 397

Qy     238 tcagaagatggcactcactgcatttatagaattttgagactccatgaaaatgcagatttt 297
Db     398 TCAGAAGACAGCACTCACTGCTTTTATAGAATCCTGAGACTCCATGAAAACGCAGGTTTG 457

Qy     298 caagacacaactctggagagtcaagatacaaaattaatacctgattcatgtaggagaatt 357
Db     458 CAGGACTCGACTCTGGAGAGTGAAGACAC------ACTACCTGACTCCTGCAGGAGGATG 511

Qy     358 aaacaggcctttcaaggagctgtgcaaaaggaattacaacatatcgttggatcacagcac 417
Db     512 AAACAAGCCTTTCAGGGGGCCGTGCAGAAGGAACTGCAACACATTGTGGGGCCACAGCGC 571

Qy     418 atcagagcagagaaagcgatggtggatggctcatggttagatctggccaagaggagcaag 477
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Qy     478 cttgaagctcagccttttgctcatctcactattaatgccaccgacatcccatctggttcc 537
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Qy     658 atttgctttcgacatcatgaaacttcaggagacctagctacagagtatcttcaactaatg 717
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Qy     718 gtgtacgtcactaaaaccagcatcaaaatcccaagttctcataccctgatgaaaggagga 777
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Qy     778 agcaccaagtattggtcagggaattctgaattccatttttattccataaacgttggtgga 837
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Qy     898 gatccggatcaggatgcaacatactttggggctttaaagttcgagatatagattga 954
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